REMARKS

Reconsideration and allowance are respectfully requested.

Claims 9-17 are pending. Non-elected claims 1-8 were withdrawn from consideration by the Examiner. Applicants cancel the non-elected claims without prejudice to future prosecution of that subject matter.

35 U.S.C. 103 – Nonobviousness

To establish a case of prima facie obviousness, all of the claim limitations must be taught or suggested by the prior art. See M.P.E.P. § 2143.03. Obviousness can only be established by combining or modifying the prior art teachings to produce the claimed invention if there is some teaching, suggestion, or motivation to do so found in either the references themselves or in the knowledge generally available to a person of ordinary skill in the art. See, e.g., *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988); *In re Jones*, 21 USPQ2d 1941, 1943-44 (Fed. Cir. 1992). Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 9-12 and 14-16 were rejected under Section 103(a) as allegedly unpatentable over Shalev et al. (Arch. Fam. Med. 5:593-596, 1996) in view of Reid (Am. J. Clin. Nutr. 73:437S-443S, 2001), Mäyrä-Mäkinen et al. (U.S. Patent 5,378,458) or Suomalinen et al. (Lait 79:165-174, 1999), and as supported by ATCC (1996). Applicants traverse.

Shalev et al. report on a study performed to determine the effect of a yogurt containing *Lactobacilus acidophilus* on bacterial vaginosis (BV) and candidal vaginitis. This study gives good results as regards bacterial vaginosis, and it is clear that the yogurt containing *Lactobacillus acidophilus* is effective against BV. In contrast, no effect on candidal vaginitis was found. Instead, on page 595, 2nd paragraph and the paragraph bridging the left and right columns, Shalev et al. unambiguously state that no statistical difference was found between the control and the test group. On page 595, Figure 2 shows even better results for the control group. The results are discussed on page 596, cautioning once again that as regards candidal vulvovaginitis, "there was no difference

between the group of patients who ate pasteurized yogurt and the group of patients who ate yogurt with viable *L. acidophilus*." In pasteurized yogurt, bacteria have been killed naturally. The results obtained, for both control and test groups, are hence speculated upon as follows: "The reason for this phenomenon could not be answered by this study: is it a placebo effect or related to yogurt ingestion per se?"

Shalev et al. hence unambiguously teach that, while a positive effect of treatment was found against bacterial infection, treatment had no effect on yeast infection. The primary reference thus teaches away from the present invention, and one of ordinary skill in the art would therefore have had no motivation to combine Shalev et al. with the other cited references with a reasonable expectation of a positive result in treating yeast infections. Therefore, Shaley et al teach away from the present invention.

Reid does not dispute the negative teachings of Shalev et al. To the contrary, he reinforces the lack of a reasonable expectation of success. As a type of infection, Reid mentions yeast vaginitis in the abstract. The review, however, reports on the effects of some probiotic agents on bacterial vaginosis, and only bacterial vaginosis. Except for the abstract, the only mention of yeast infection in Reid is in the last paragraph on page 438S, which states. "The dominant presence of lactobacilli in the urogenital microflora of healthy women and the obliteration of lactobacilli in patients who develop UTI, BV, and many other genital infections [**except candidiasis**] has led to focus on these bacteria" (citations omitted, emphasis added). Hence, Read teaches that bacterial infections and other infections of the urogenital tract are due to an imbalance in the lactobacilli in the flora, but that candidiasis does not result from such. Therefore, Read also teaches away from the present invention.

As mentioned in the Action, both Mäyrä-Mäkinen et al. and Suomalainen et al. relate to the use of *Lactobacillus casei* ssp. *rhamnosus* LC705, DSM 7061 in combination with *Propionibacterium freudenreichii* ssp. *shermanji* PJS, DSM 7067 as natural biopreservatives in the food industry. Both documents are, however, totally silent as regards any sort of therapeutic treatment of human individuals. Shalev et al. and Reid, on the other hand, teach away from the present invention by disclosing that such treatment would have no positive effect on yeast infections. One of ordinary skill in the art

would thus have had no motivation at the time Applicants' invention was made to combine Shalev et al. with the secondary references in hope of a positive result.

Example 1 of the present application shows that the combination of the invention is effective against yeast infections, and produces statistically significant results both in patients with high and relatively high yeast counts (paragraph [0067]). Such an effect is quite surprising in view of Shalev et al. or Reid, which both teach that no effect against yeast infection is obtained by treatment with lactobacilli.

Claims 9-17 were rejected under Section 103(a) as allegedly unpatentable over Shalev et al. (Arch. Fam. Med. 5:593-596, 1996) in view of Reid (Am. J. Clin. Nutr. 73:437S-443S, 2001), Mäyrä-Mäkinen et al. (U.S. Patent 5,378,458) or Suomalinen et al. (Lait 79:165-174, 1999), and as supported by ATCC (1996) as applied to claims 9-12 and 14-16, and further in view of Vinderola et al. (J. Dairy Sci. 83:1905-1911, 2000) and Simons et al. (Caries Res. 31:91-96, 1997). Applicants traverse.

The negative teachings of Shaley et al. and Reid are not contradicted by Vinderola et al. and Simons et al. For the reasons explained above, one of ordinary skill in the art thus would not have been motivated to combine the references as proposed by the Examiner or had a reasonable expectation of success.

Withdrawal of the Section 103 rejections is requested because the invention as claimed would not have been obvious to one of ordinary skill.

Double Patenting

Claims 9-17 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being allegedly unpatentable over claims 1-14 of co-pending Application No. 10/470,151. Applicants traverse.

The present invention relates to a combination of three bacteria: *Lactobacillus rhamnosus* LGG, ATCC 53103; *Lactobacillus rhamnosus* LC-705, DSM 7061; and *Propionibacterium shermanji* PJS, DSM 7067. The invention of claims 1-14 of Application No. 10/470,151 further requires the use of a bacterium belonging to the species *Bifidobacterium*.

The present invention is based on a newly discovered effect of the recited probiotic combination, namely its ability to inhibit yeast growth in vivo. Therefore, the combination is useful for the preparation of a product for treating or preventing disorders caused by yeast or for relieving yeast-related symptoms in humans and animals.

In contrast, claims 1-14 of Application No. 10/470,151 describe different therapeutic purposes. According to page 8 of the specification [0029] to [0030]:

> "The new combination can be used as such or as a part of another product, such as a pharmaceutical or a food product. The combination of the invention has an advantageous effect on the human intestinal balance in that it increases the entero-lactone production and reduces a disadvantageously high pH value. The combination also influences the immune response by increasing the amount of lymphocytes and that of γ-interferon (IFN) and by reducing the formation of carcinogenic substances. The combination of the invention is thus useful for the prevention and treatment of intestinal disorders, allergies and cancer and for promoting general health.
>
> In accordance with the present invention, the combination is thus also applicable as a therapeutic substance and in the preparation of therapeutic substances."

Therefore, "inhibiting the growth of yeasts and for relieving yeast-related symptoms in animals or humans" as required by the present claims is neither taught nor suggested by claims 1-14 of Application No. 10/470,151.

Withdrawal of the double patenting rejection is requested.

Conclusion

Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect.

Respectfully submitted,

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